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JUL 14 2005

TRANSMITTAL OF APPEAL BRIEF (Small Entity)

Docket No.
MSU 4.1-587

Re: Application Of: Evangelyn C. Alocilja and Zarini Muhammad-Tahir

| Application No. | Filing Date | Examiner | Customer No. | Group Art Unit | Confirmation No. |
|-----------------|-------------------|-------------|--------------|----------------|------------------|
| 10/074,499 | February 13, 2002 | Leon Y. Lum | 21036 | 1641 | 4246 |

Invention: CONDUCTIMETRIC BIOSENSOR DEVICE, METHOD AND SYSTEM

COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on:
July 12, 2005

☒ Applicant claims small entity status. See 37 CFR 1.27

The fee for filing this Appeal Brief is: \$250.00

☒ A check in the amount of the fee is enclosed.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 13-0610

☐ Payment by credit card. Form PTO-2038 is attached.

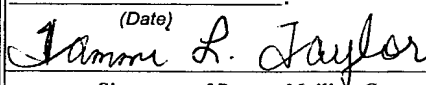
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Dated: 07/12/2005

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| I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on 07/12/2005 (Date)  Signature of Person Mailing Correspondence Tammi L. Taylor Typed or Printed Name of Person Mailing Correspondence | |
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MSU 4.1-587
Appl. No. 10/074,499
July 11, 2005
Appeal Brief



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/074,499 Confirmation No. 4246
Applicants : Evangelyn C. Alocilja and
Zarini Muhammad-Tahir
Filed : February 13, 2002
TC/A.U. : 1641
Examiner : Leon Y. Lum
Docket No. : MSU 4.1-587
Customer No. : 21036

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF UNDER 37 C.F.R. § 41.37

Sir:

This is an appeal from a final rejection in the above entitled application. The claims on appeal are set forth as Claims Appendix. An oral hearing will be requested. Enclosed is the fee due upon filing of the Brief.

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(1) Real Party in Interest

The real party in interest is the Board of Trustees operating Michigan State University, East Lansing, Michigan, a constitutional corporation of the State of Michigan, which is the assignee of the above entitled application.

(2) Related Appeals and Interferences

There are no pending related appeals and interferences.

(3) Status of Claims

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are pending in the application. Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 were rejected. Claims 4-6, 11-13, 17, 20, 23 and 25 were subject to a restriction requirement and were canceled in the prosecution. No claims have been allowed.

(4) Status of Amendments

An Amendment under 37 C.F.R. 1.116 was mailed on June 08, 2005. The amendment was entered.

(5) Summary of Claimed Subject Matter

The claimed subject matter in Claim 1 is a biosensor device (Support for this Claim is found at page 3, line 16 through page 4, line 6 of the specification; illustrated in Figures 1A-1E) which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first capture reagent (page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer (page 9, line 12 through page 10, line 1 of the

specification), wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex (page 10, lines 8-9 of the specification) in absence of electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte. The operation of the biosensor device is illustrated in Figures 2A-2C1 as described at page 11, lines 7-18.

The claimed subject matter in Claim 7 is a system for detecting an analyte in a fluid sample (Support for this Claim is found at page 5, line 7 through page 6, line 4 of the specification) which comprises:

(a) a biosensor device which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first capture reagent (page 9, lines 4-11 of the specification) bound to the

substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer (page 9, line 12 through page 10, line 1 of the specification) wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex (page 10, lines 8-9 of the specification) in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the analyte (digital multimeter 19 in Figure 6A as described at

page 18, lines 23-28; and Figure 4 as described at page 19, line 22 through page 20, line 1). The operation of the biosensor device is illustrated in Figures 2A-2C1 as described at page 11, lines 7-18.

The claimed subject matter in Claim 8 is a biosensor device (Support for this Claim is found at page 6, lines 5-25 of the specification illustrated in Figures 1A-1E) which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first antibody (capture reagent of page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area (immobilization of antibody on page 17, lines 3-17) for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer

(antibody labeling with polyaniline on page 16, lines 11-20; page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an antigen which is bound by the second antibody, bound to the conductive polymer, forms a complex in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the antigen (analytical procedure on page 18, lines 6-28).

The claimed subject matter in Claim 14 is a system for detecting an antigen in a fluid sample (Support for this Claim is found at page 7, line 25 through page 8, line 22 of the specification illustrated in Figures 1A-1E) which comprises:

(a) a biosensor device which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first antibody

(capture reagent of page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area (immobilization of antibody on page 17, lines 3-17) for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer (antibody labeling with polyaniline on page 16, lines 11-20; page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an antigen which is bound by the second antibody, bound to the conductive polymer, forms a complex in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes (analytical procedure on page 18, lines 6-28);

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the antigen (digital multimeter 19 in Figure 6A as described at page 18, lines 23-28; and Figure 4 as described at page 19, line 22 through page 20, line 1).

(6) Grounds of Rejection to Be Reviewed on Appeal

(a) Claims 1-2, 7-9, 14-16, 18-19 and 21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Manz et al. (WO 00/03233).

(b) Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Manz et al. (WO 00/03233), and further in view of Roberts et al. (U.S. Patent No. 5,958,791).

(7) Argument

A. The Examiner rejected Claims 1-2, 7-9, 14-16, 18-19 and 21 under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (*Biosensors & Bioelectronics* 2000, 14: 907-915) in view of Manz et al. (WO 00/03233). In particular, it was stated in the rejection that one of ordinary skill in the art at the time of the invention would have had a "reasonable expectation of success" in modifying the device of Kim et al. with the conductive polymer beads having a molecular probe immobilized on the bead surface taught by Manz et al.

To establish a *prima facie* case of obviousness, basic criteria must be met. There must first be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. This teaching or suggestion to make the claimed combination must be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). There is no teaching or suggestion to modify the cited references or combine the

reference teachings so as to provide the claimed biosensor device.

Kim et al. discloses a conductimetric membrane strip immunosensor for the detection of human serum albumin (HSA) as an analyte. Kim et al. teaches the use of antibodies against the HSA analyte which have been conjugated to colloidal gold particles as a signal generator for the conductimetric immunosensor. Kim et al. teaches first to affinity purify antibodies against human serum albumin (HSA) and then to conjugate the affinity purified antibodies with colloidal gold particles. (Kim et al. page 908, last paragraph). The colloidal gold-antibody conjugate is added to a site on the glass fiber membrane before adding an aqueous sample containing the HSA analyte. The sample is absorbed by capillary action into a membrane strip system which is illustrated in Figure 1. The colloidal gold-antibody conjugate binds the analyte to form a complex which travels up the strip to a signal generation pad where an immobilized antibody, also against the HSA analyte, binds the analyte in the complex. The colloidal gold particles captured on the signal generation pad result in a colored signal which can be quantified by optical density values.

(Kim et al. page 910, second column, last paragraph).

As an alternative to this colorimetric method of detection, " the density of particulate gold, electron-rich metal, can be determined by measuring electric conduction." (Kim et al.: page 911, section 3.2, first paragraph). Kim et al. teaches placement of two electrodes in the region where the immobilized antibodies bind the analyte in the complex. Since the immobilized antibodies bind the analyte in the complex between the two electrodes, electrical conductivity was monitored. Kim et al. teaches however, that the conductivity signal is "so weak that the maximum signal-to noise ratio was approximately two times lower than the value determined by the photometry. The dose-response curves further revealed that the monitoring based on conductimetry involved a comparatively large variation." (Kim et al.: page 911, right column, second paragraph).

Kim et al. teaches that with the plain gold particles, poor analytical performances in generating the conductimetric signal "could result from an impaired transfer of electrons along the gold particles spread on the membrane surface." (Kim et al. "Discussion", page 913, first paragraph). After conjugating the gold particles to

the antibody the "residual surfaces of the gold particles were blocked by adding 0.1 M Tris, pH 7.6, containing 5% casein (1 ml) for 30 min." (Kim et al. sentence spanning page 908 and page 909). Kim et al. adds the casein as a protein blocking layer for reducing non-specific interactions with the gold particles. Kim et al. teaches that since the gold particles are surrounded with protein molecules, i.e. immunoglobulin and casein as blocking agent for reducing non-specific interactions, an ionic polymer shell is rendered on the outside of the gold. (Kim et al. "Discussion", page 913, first paragraph). "This ionic polymer shell may interfere with electron hopping, a dominant process of charge-transfer between the conducting mediators." (Kim et al. page 913, first paragraph of right column) Kim et al. further states that because "protein molecule could behave similarly to amorphous semiconductor, the shell thickness exceeding the distance required for efficient electron relay acts as a barrier against conduction." Kim et al. initially attempted to resolve the conduction barrier problem by using an external blocking molecular layer of polyethylene glycol instead of the casein. However, Kim et al. conclude:

"Under the given conditions, the signal-to-noise ratio was enhanced by 30% as compared with the ionic protein coating, however the performance was still inferior to that of colorimetric detection. Therefore, it was concluded that the conductimetric analysis was relatively insensitive and was unsuitable for the system employing the conventional gold colloids as label."

(Kim et al.: first paragraph of Discussion, page 913).

Kim et al. then takes a different approach in an attempt to resolve the problem due to the electronic barrier surrounding the gold. After combining the antibody solution with the gold particles for conjugation, Kim et al. "introduced, on the surface, polymeric conductor molecules that may bridge the neighboring particles or at least bring them closer to improve the charge-transfer state." Kim et al. uses polyaniline as the polymeric conductor molecule. "[P]olyaniline solutions diluted with PB in different concentrations (0.01-1 mg/ml) were added into the mixtures of gold and antibody and then reacted for 30 min." Kim et al. teaches that "[w]hen the polyaniline solution is added to the gold suspension, the molecules diffuse to the particle surface and subsequently adsorb to form an ordered layer on the residual sites after the antibody coating." (Kim et al.: page 913, right column, last paragraph). An illustration of the polyaniline polymer adsorbed on the

surface of the gold particles is shown in the top frame of Figure 4 on page 912.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). The teachings of Kim et al. would have suggested to those of ordinary skill in the art to keep the gold particles. In an attempt to resolve the electronic barrier problem, Kim et al. did not in any way suggest removing the gold particles but rather to introduce polymeric conductor molecules to improve the charge transfer between the gold particles. As taught by Kim et al. the "protrusion degree of the polymer strands, acting as a wire (i.e. molecular wires) for electrical connection, outside from the surface (refer to the top of Fig. 4) mainly depends on the polymer concentration applied and the molecular dimension." (Kim et al.: page 913, right column, last paragraph). The "extended filaments of the polymer in a plethora cross-linked the particles." (Kim et al.: page 913, right column, last paragraph).

Kim et al. makes it clear that the gold particles

are important for the generation of the biosensor signal. One advantage of having the gold particles surfaces as taught Kim et al. is that "the presence of polymer strands on the surfaces may result in a high interfacial capacitance and, thus, a gain of conduction." (Kim et al.: first full paragraph, page 914). Kim et al. teaches that interfacial capacitance due to the presence of polymer strands on the surface of the gold particles is a major contributor to signal generation in a low range of the gold concentration.

"In a low range of gold concentration, the conductimetric signal increased in approximate proportion to the optical density, which could indicate the interfacial capacitance as a major contribution to the signal generation."

(Kim et al.: first full paragraph, page 914). This knowledge would not lead a person of skill in the art to remove the gold particles and directly conjugate the antibody or other capture reagent directly to the polymeric conductor molecules. This teaching of an interfacial capacitance would actually strongly suggest that the gold particles are important components of the system, since the surface of the gold particles can generate an interfacial capacitance which contributes to the signal generation.

It is improper to combine references where the

references teach away from their combination. In *re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Kim et al. teach the strategy of using the colloidal gold-antibody conjugates with the conducting polymer and not the direct labeling of the antibody with the conducting polymer by chemical reaction "because, in such a case, the protein molecule itself does not contain available sites for electron relay." (Kim et al.: Conclusions, page 914). Therefore, one skilled in the art reading Kim et al. would be directed away from eliminating the metal (gold) particles since Kim et al. teaches that direct labeling of the antibody with the polymer would not have the electron relay sites on the antibody protein molecule which are necessary for conduction.

It was stated in the rejection that it would have been obvious to substitute the metal bead of Kim et al. with the polymer bead of Manz et al. since the polymer bead is able to perform the same functions as the metal bead. Manz et al. disclose an electrochemiluminescence apparatus with floating reaction electrodes. The electrochemiluminescence apparatus comprises a reaction vessel, a means for generating an electric field within at least a region of the

reaction vessel, and one or more electrodes in the field arranged to float in or on a solution in the reaction vessel. Manz et al. further teach that bioassays can be carried out by preparing small batches of metal, metal coated or conductive polymer beads with a specific molecular probe immobilized on the bead surface. Since Manz et al. do not teach a biosensor device similar to the claimed invention, Manz et al. in no way shows or suggests using the polymer bead as a substitute for the gold particles of Kim et al. Using the polymer beads of Manz et al. in place of the gold particles of Kim et al. does nothing to solve the conductivity problems associated with using the gold beads which Kim et al. attempts to resolve. There is nothing to motivate a person of ordinary skill in the art to use conductive polymer beads instead of the gold particles described by Kim et al.

According to MPEP 2144.06, in order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ

340 (CCPA 1958); *In re Scott*, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another.) Even if the polymer beads of Manz et al. were able to perform the same function as the gold particles of Kim et al., using conductive polymer beads is not an obvious modification in view of the gold particles of Kim et al. There is no suggestion to make the combination of the device of Kim et al. with functionally or mechanically equivalent conductive polymer beads in any of the cited prior art.

There is nothing in the references which would suggest the desirability using conductive polymer beads, since the using conductive polymer beads do nothing to address the problems which are associated with using the gold particles of Kim et al. Nothing in the cited references would suggest that it would no longer be necessary to block the bead surfaces with protein molecules as a blocking agent for reducing non-specific interactions

with the bead. Therefore, an ionic polymer shell would still be rendered on the bead surfaces upon addition of the protein molecules. This ionic polymer shell would still cause a conduction barrier similar to the one described by Kim et al. Using polymer beads in place of the gold particles of Kim et al. does nothing to solve the conductivity problems associated with using the gold beads. A person of ordinary skill in the art would recognize that replacing the gold particles with a polymer bead does not lead to a solution to the conductivity problem, and therefore the person of skill in the art would have no motivation to modify the references in this manner.

One consideration which applies to obviousness rejections is that the references must be viewed without the benefit of hindsight vision afforded by the claimed invention. "It is difficult but necessary that the decision maker forget what he or she has been taught . . . about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." *W.L. Gore & Associates, Inc.*

v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Replacing the gold particles of Kim et al. with the conductive polymer beads of Manz et al. in place of the gold particles appears to be an example of using impermissible hindsight reasoning. Nothing in Kim et al. would suggest replacing the gold particles with a conductive polymer bead. Manz et al. teach a completely unrelated electro-chemiluminescence apparatus with floating electrodes and as such adds nothing to motivate a person of skill in the art to make the combination in the claimed biosensor device. Therefore, the cited references when viewed as a whole do not suggest the desirability and thus the obviousness of making this combination.

B. The Examiner rejected Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (Biosensors & Bioelectronics 2000, 14: 907-915) in view of Manz et al. (WO 00/03233), and further in view of Roberts et al. (U.S. Patent No. 5,958,791).

Claims 3, 10, 22, 24 and 26 are patentable over Kim et al. and Manz et al. for the reasons discussed above. Additionally, with regards to Claims 22, 24 and 26, Kim et al. and Manz et al. further fail to teach a multiple array of devices so that multiple analytes are detected simultaneously from the same sample. Roberts et al. teaches test devices including multiple sets of interdigitated electrode arrays for simultaneous multiple analyte detection and assay of a test sample for a plurality of analytes. However, Roberts et al. does not teach a *single* multiple array as taught by Applicants as illustrated in Figure 3. The simultaneous multiple analyte detection taught by Roberts et al. uses multiple sets of interdigitated electrode arrays in order to perform simultaneous multiple analyte detection to assay the test sample for a plurality of analytes. The liposome-enhanced immunoassay and test device taught by Roberts et al. would not suggest to a

person of ordinary skill in the art the single multiple array as taught by Applicants, since the nature of the immunoassay and test device taught by Roberts et al. requires separate competitive binding portions 104 and measurement portions 106. The test of Roberts et al. requires that a test mixture with the analyte of interest first passes through a competitive binding portion 104 having the binding material for the analyte before passing through a liposome lysing portion 106 where a liposome lysing agent releases the electroactive marker from the liposome. The electroactive marker is then carried by the migrating mixtures, via capillary action, into and through the electrochemical measurement portion to complete the electrical circuit (Roberts et al.: col. 15, line 53 through col. 16, line 5). A single multiple array as taught by Applicants and illustrated in Figure 3, wherein a plurality of analytes in a mixture can each be individually detected at one of the multiple regions 21A to 21D would not be suggested by the cited prior art references. In the embodiment illustrated in Figure 3, each one of the analytes bind to a specific capture reagent/antibody at one of the zones between the electrodes to generate a signal at one of

the regions 21A-21E representative of that particular analyte. Each analyte will generate one of an array of simultaneous voltage signals 33 which is proportional to the change of the resistance in that region. The immunoassay and test device taught by Roberts et al. does not show or suggest such an array, since specific binding must be completed *before* the test mixture flows between the electrodes in the measurement portion 106. If the adjacent electrodes are spaced too closely together in the immunoassay and test device taught by Roberts et al., the electroactive marker can diffuse over to an adjacent region to generate a false signal in that region. Due to this possibility, the electrode arrays of Roberts et al., unlike those arrays taught by Applicants, must be maintained at a large enough distance so that no electroactive markers can diffuse over the electrodes in an adjacent measurement portion 106. The design of the device taught by Applicants does not have this problem with cross over signal. Since only the first capture reagent specific for the desired analyte is present between the electrodes only the desired complex of the analyte and second capture reagent bound to the electrically conductive polymer will be bound between

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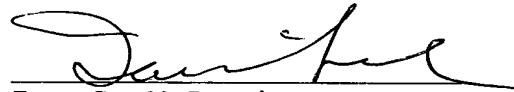
the electrodes. Therefore any signal measured across the electrodes of any of the regions 21A to 21D is generated by specific binding of the desired analyte to the region.

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C. Conclusion

As shown above, the device and system of the present invention is not obvious over the cited prior art references. Therefore, Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are each patentable. Reversal of the Final Rejection is requested.

Respectfully,



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CLAIMS APPENDIX

A biosensor device which comprises:

a strip of a substrate having at least two zones wherein

a

(1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer, wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex in absence of electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte.

2. The device of Claim 1 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

3. The device of any one of Claims 1 or 2 wherein the first defined area has a dimension between the electrodes of 1.0 mm or less.

7. A system for detecting an analyte in a fluid sample which comprises:

(a) a biosensor device which comprises:

a strip of a substrate having at least two zones wherein
a

(1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive

polymer wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the analyte.

8. A biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first antibody bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer

medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer, wherein when a fluid sample containing an antigen which is bound by the second antibody, bound to the conductive polymer, forms a complex in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the antigen.

9. The device of Claim 8 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

10. The device of any one of Claims 8 or 9 wherein the first defined area has a dimension between the electrodes of 1.0 mm or less.

14. A system for detecting an antigen in a fluid sample which comprises:

(a) a biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first antibody bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer, wherein when a fluid sample containing an antigen which is bound by the second antibody, bound to the conductive polymer, forms a complex in absence of any electrically conductive metal particles in the complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias

between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the antigen.

15. The system of Claim 14 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

16. The device of Claim 1 or 2 wherein a third zone adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

18. The system of Claim 7 or 8 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

19. The device of Claim 8 or 9 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

21. The system of Claim 14 or 15 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

22. The device of Claim 1 or 2 as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the same sample.

24. The device of Claim 8 or 9 as a multiple array of devices grouped together separately on the substrate so that multiple analytes are detected simultaneously from the same sample.

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26. The system of Claim 14 or 15 as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the sample.